

**REMARKS**

Applicants submit that the amendments and new claims presented herein are fully supported in the present specification as filed and add no new matter. Further, it is respectfully requested that the present Amendment be entered into the Official File in view of the fact that the Amendment automatically places the application in condition for allowance.

Applicants further note that the amended claims and new claims presented herein present no new issues requiring further search or consideration because many of the claims of the same or similar scope have previously been presented and subsequently examined. For instance, the scope of claims 6 and 7 as amended herein have clearly been considered before since these two claims now depend on even less claims.

Alternatively, if the Examiner continues with the rejections of the present application, it is respectfully requested that the present Amendment be entered for purposes of an Appeal.

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims.

***Status of the Claims***

Claims 1-7 and 10-14 are pending. Claims 8 and 9 were previously canceled. In the present Amendment, claims 1, 6, 7 and 10 have been amended herein. Also, claims 11-14 have been added.

Support for the amendments to claims 1 and 10 as well as for new claims 11-14 can be found in the Examples of the present specification, especially from page 22, line 20 to page 23,

line 12; page 25, lines 9-17, page 27, lines 5-14; page 35, lines 6-21; and page 42, line 21 to page 43, line 11. The amendments to claims 6 and 7 are made to change the dependencies thereof.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims. The outstanding rejections are newly formed, and thus the remarks below address the new rejections.

***Issues Under 35 U.S.C. § 103(a)***

Claims 1, 2, 3, 6 and 10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.* (*J. Biol. Chem.*, Vol. 268, p. 20443-20451 (1993)) in view of Blain *et al.* (*J. Biol. Chem.*, Vol. 272, p. 25863-25872 (1997)), Jeong and Nikiforv (*BioTechniques*, Vol. 27, p. 1232-1238, (1997)) and Facemyer and Cremo (*Bioconjug. Chem.*, Vol. 3, p. 408-413 (1992)) (see paragraph 3 of the outstanding Office Action).

Also, claims 1 and 4 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.*, Jeong and Facemyer and Cremo and in further view of Hemmila (*Clin. Chem.*, Vol. 33, p. 359-370 (1985)) (see paragraph 4 of the Office Action).

Further, claims 1 and 5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.*, Jeong and Facemyer and Cremo, in further view of Strachan and Read (*Human Molecular Genetics*, BIOS Scientific Publishers Ltd., Section 20.2.5 (1999)) (see paragraph 5 of the Office Action).

These rejections are respectfully traversed. Reconsideration and withdrawal thereof are respectfully requested.

Distinctions over the First Combination of Pan, Blain, Jeong, and Facemyer: Instantly Pending  
Claims 1, 2, 3, 6 and 10

The cited Pan *et al.* reference describes a method for measuring activities of cdk2 and cdc 2 purified from HeLa cells. However, Applicants respectfully refer the Examiner to the scope of claim 1 as presented herein. As can be seen, the primary reference Pan is silent on a method comprising steps of catching CDK with an anti-cyclin-dependent kinase antibody, reacting ATP- $\gamma$ S with a substrate, placing the reacted substrate on a membrane, coupling a labeling fluorophore or a labeling enzyme with a sulfur atom of the reacted substrate on the membrane, washing the membrane, measuring the amount of fluorescence, or reacting the labeling enzyme with a substance and measuring the amount of the generated product, and calculating the activity of CDK as recited in the present claim 1. Still, the Examiner refers Applicants to the disclosure in the cited secondary references to form the instant rejection.

The cited secondary reference of Blain *et al.* (newly cited) relates to a method of measuring CDK activity in mink lung epithelial cell line (Mv1Lu). However, the Blain reference fails to disclose a method comprising steps of catching CDK with an anti-cyclin-dependent kinase antibody, reacting ATP- $\gamma$ S with a substrate, placing the reacted substrate on a membrane, coupling a labeling fluorophore or a labeling enzyme with a sulfur atom of the reacted substrate on the membrane, washing the membrane, and calculating the activity of CDK as stated in

instantly pending claim 1.

The cited Jeong *et al.* reference discloses a method for measuring the activity of protein kinase A which is commercially available. The substrate, kemptide, is labeled with FITC prior to the reaction of the substrate with protein kinase A and ATP- $\gamma$ S.

On the other hand, the substrate used in the present invention is labeled with the fluorophore or enzyme after the reaction of the substrate with the activated CDK and ATP- $\gamma$ S. Therefore, one of ordinary skill in the art would not obtain the present invention by combining Pan with the method disclosed in Jeong. Indeed, the combination of Pan and Blain with Jeong is improper. This is because, as just one instance, Jeong discloses using a substrate (kemptide) labeled with FITC prior to the reaction of the substrate with protein kinase A and ATP- $\gamma$ S. But in the present invention, the substrate is labeled with the fluorophore or enzyme after the substrate's reaction with the activated CDK and ATP- $\gamma$ S.

Moreover, the secondary reference of Jeong is silent with respect to a method comprising the steps of catching CDK with an anti-CDK antibody, placing the reacted substrate on a membrane, coupling a labeling fluorophore or a labeling enzyme with a sulfur atom of the reacted substrate on the membrane, and washing the membrane, as instantly recited in pending claim 1. The deficiencies of this reference are the same as Pan and Blain. Still, the Examiner refers Applicants to the fourth secondary reference of Facemyer.

The other cited secondary reference of Facemyer and Cremo discloses a method for measuring the activity of myosin light chain kinase after isolation and purification of the same. In the second paragraph of the left column on page 408 of this document, kinases are disclosed

as being known to use ATP- $\gamma$ S as a substrate. These kinases include phosphorylase kinase, cAMP dependent protein kinase, nuclear protein kinase II, cGMP dependent protein kinase, protein kinase C, kinase FA, heme-regulated protein kinase, myosin light chain kinase, calmodulin-dependent protein kinase II, and EGF-receptor-associated protein kinase.

However, the cited Facemyer document fails to disclose CDK as used in the present invention. Therefore, one of ordinary skill in the art would not be motivated to combine the disclosure of Facemyer and Cremo with Pan, Blain and Jeong and Nikiforv to obtain the present invention. In addition, the Facemyer reference is silent regarding any description of a method comprising the steps of catching CDK with an anti-cyclin-dependent kinase antibody, reacting ATP- $\gamma$ S with a substrate, placing the reacted substrate on a membrane, coupling a labeling fluorophore or a labeling enzyme with a sulfur atom of the reacted substrate on the membrane, washing the membrane, and calculating the activity of CDK as the present claim 1.

Therefore, claims 1, 2, 3, 6 and 10 are not *prima facie* obvious over Pan *et al.* in view of Blain, Jeong and Facemyer. U.S. case law squarely holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *see also In re Kotzab*,

55 U.S.P.Q.2d 1313, 1316-17 (Fed. Cir. 2000). Here, not even the initial requirement of disclosure of all claimed features has been satisfied. The cited combination of references fails to disclose, e.g., the use of CDK such as the catching, reacting, placing, coupling and washing steps (see pending claim 1). Thus, a *prima facie* case of obviousness has not been established and this rejection has been overcome.

Further, the requisite motivation is lacking. In this regard, it is not *prima facie* obvious to modify a reference unless the references suggest an advantage to be gained from the modification. *See In re Sernaker*, 217 USPQ 1, 6 (Fed. Cir. 1983). Moreover, the cited references must suggest the desirability of the modification. *In re Brouwer*, 37 USPQ2d 1663, 1666 (Fed. Cir. 1995). The cited references do not suggest any advantage to be gained by making the Examiner's proposed combination. Here, as just one instance, Pan, Blain and Jeong fail to disclose catching CDK with an-CDK antibody and Facemyer and Cremo fails disclose anything regarding CDK as instantly claimed. Thus, under *Vaeck*, *Sernaker* and *Brouwer*, the requisite motivation is lacking and this rejection has been overcome. More specifically, the references do not suggest any advantage of catching CDK with an anti-cyclin-dependent kinase antibody, reacting ATP- $\gamma$ S, etc., as instantly claimed.

Thus, this rejection has been overcome since a *prima facie* case of obviousness has not been established. Reconsideration and withdrawal of this rejection are respectfully requested.

Distinctions over the Second Combination of Pan, Jeon, Facemyer and Hemmila: Instantly Pending Claims 1 and 4

Pan is discussed above. The secondary reference of Hemmila discloses a fluoroimmunoassay using FITC as a fluorescent label for substrates. However, Hemmila is silent for catching CDK in the sample by anti-CDK antibody, reacting ATP- $\gamma$ S with a substrate in the presence of CDK, and calculating the activity of CDK as the present claim 1. Thus, the instant combination of Pan, Jeon and Facemyer, and further with Hemmila is improper. There is no disclosure of all claimed features since not all instantly recited steps are met by the cited combination of references. *In re Vaeck; supra*. Thus, this rejection has been overcome and withdrawal thereof is respectfully requested.

Distinctions over the Third Combination of Pan, Jeong, Facemyer and Strachan: Instantly Pending Claims 1 and 5

Similar to the other two rejections discussed above, a *prima facie* of obviousness has not been established since each of the cited references, including Strachan and Read, fails to disclose all instantly claimed steps as recited in pending claim 1 (wherein disputed claim 5 depends on claim 1). *In re Vaeck; supra*. Though the secondary reference of Strachan and Read may disclose expression mapping and the use of a peroxidase as a protein label, this document fails to disclose the instantly claimed method for calculating the activity of CDK.

As stated above, because the present claim 1 is not *prima facie* obvious over Pan et al. in

view of Jeong and Nikiforv and Facemyer and Cremo, the present claims 1 and 5 are not *prima facie* obvious combining Strachan and Read. Reconsideration and withdrawal of this rejection are respectfully requested.

***Information Disclosure Statement***

Applicants note that an Information Disclosure Statement was filed on December 2, 2005. Applicants respectfully request consideration of each of the cited references, as well as return of a copy of the initialed PTO/SB/08a/b form.

***Conclusion***

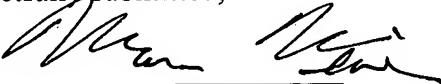
A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact Eugene T. Perez (Reg. No. 48,501) at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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